CLAIMS:

1. ~~A method for distinguishing between two known single nucleotide variants~~ of a single stranded oligonucleotide target ~~sequence~~ which comprises:

(i) providing a single stranded oligonucleotide sequence having one or the other of said two known nucleotide variants,

each of said variants of said target sequence having an identical first flanking sequence immediately adjacent one side of said single variant nucleotide and an identical second flanking sequence immediately adjacent the other side of said single variant nucleotide;

(ii) providing first and second oligonucleotide substrate sequences complementary respectively to said first and second single variant nucleotide flanking sequences of said target sequence;

(iii) hybridizing said first and second single variant nucleotide flanking sequences, with said respectively complementary first and second substrate sequences to provide a duplex consisting of said target sequence having said substrate sequences hybridized thereto in head to tail juxtaposition; and

(iv) subjecting said duplex to conditions effective to ligate said substrate sequences but only in the absence of a mismatch between the target sequence and the ligated substrate at the ligation junction.

2. A method as defined by claim 1 in which said substrate sequences are 8 to 25 nucleotides in length.

3. A method as defined by claim 1 or claim 2 in which sodium chloride at a concentration of 200 mM to 500 mM or spermidine in a concentration of 2 to 5 mM is present in the ligation reaction mixture utilized in step (iv).

4. A method as defined by claim 1 in which the step (iv) conditions effective to ligate said substrate sequences include the use of T4-DNA ligase, E. Coli DNA ligase or thermophilus ligase.

5. A method for amplifying a nucleic acid comprising a target sequence comprising the steps of:

(i) generating a single-stranded template comprising the target sequence;

(ii) hybridizing a pair of oligonucleotides to the template such that the oligonucleotides are juxtaposed for ligation on the template and each oligonucleotide is positioned to flank the target sequence;

(iii) ligating the juxtaposed oligonucleotides to produce a double-stranded ligation product;

(iv) denaturing the double stranded ligation product to produce an initial template strand and an oligonucleotide ligation product strand; and

(v) repeating steps (ii) (iv) such that both the initial template strand and the oligonucleotide ligation strand act as templates for a further ligation reaction.

6. A method according to claim 5 wherein the single stranded template is generated by disassociating the complementary strands of a double-stranded nucleic acid.

7. A method according to claim 6 wherein both complementary strands are used as templates.

8. A method according to any one of claims 5 to 7 wherein the nucleic acid is DNA.

9. A method according to any one of claims 5 to 7 wherein the nucleic acid is RNA.

10. A method according to any one of claims 5 to 8 wherein the target sequence is a single nucleotide.

11. A method according to claim 5 further comprising producing an amplification product by repetition of step (v) and subsequently determining the presence or absence of a nucleic acid sequence complementary to or identical to the target sequence in the amplification product.

12. A method for amplifying at least one specific nucleic acid sequence in a sample containing a nucleic acid or a mixture of nucleic acids comprised of single or complementary nucleic acid strands, wherein said sample is suspected of containing said at least one specific sequence comprising:

(a) treating the strands with at least one of two pairs of oligonucleotides which sets are complementary to at least one said specific nucleic acid sequence and flank at least one target base of a single stranded template or at least one target base pair defining a blunt end contained in said nucleic acid sequence or sequences wherein one end nucleotide of one of the oligonucleotides of at least one of said pairs is complementary to said target base or one of the bases of said target base pairs under conditions such that said end nucleotide will mutually ligate with an end of the other oligonucleotide of said pair to form a ligation product which is complementary to said specific nucleic acid sequence if said target base or target base pair is present in said sample;

(b) treating said sample under conditions to separate ligation products from their templates if said target base or target base pairs to be detected are present in said sample; and

(c) determining whether ligation has occurred.

13. The method of claim 12 wherein steps (a) and (b) are repeated at least once.

14. The method of claim 12 wherein a nucleic acid sequence is treated with said two pairs of oligonucleotides, and said ligation product of one of said pairs of oligonucleotides, when separated from its complement, can serve as a template for the other pair of oligonucleotides and result in an exponential formation of ligation product.

15. The method of claim 12 wherein a nucleic acid sequence is treated with only one pair of said two pairs of oligonucleotides and said ligation product of said one pair is separated from its complement and another of said pairs is ligated and hybridized to the same template resulting in a linear formation of ligation product.

16. The method of claim 12 wherein said ligation products are separated from their templates by denaturing.

17. The method of claim 12 wherein said nucleic acid is double stranded and its strands are separated by denaturing before or during step (a).

18. The method of claim 12 wherein oligonucleotides of any of said pairs of oligonucleotides comprising the 3′ end of an ultimate ligation product are phosphorylated at their 5′ ends.

19. The method of claim 12 wherein a deletion or mutation of said target base or said target base pair causes a genetic disease.

20. The method of claim 19 wherein said genetic disease is sickle cell anemia.

21. The method of claim 20 wherein said pairs of oligonucleotides comprise ON1/ON2 and ON3/ON4.

22. The method of claim 20 wherein said pairs of oligonucleotides comprise ON1/ONS2 and ONS3/ON4.

23. The method of claim 12 wherein step (a) is accomplished using an enzyme selected from the group consisting of T4 DNA ligase and E.coli DNA ligase.

24. The method of claim 12 wherein said specific nucleic acid sequence is DNA.

25. The method of claim 12 wherein said specific nucleic acid sequence is RNA.

26. The method of claim 25 wherein said specific nucleic acid sequence is RNA copied into DNA by treatment with reverse transcriptase prior to step (a).

27. The method of claim 12 wherein at least one oligonucleotide of said pairs of oligonucleotides is radiolabeled.

28. The method of claim 12 wherein the reaction mixture of step (a) further comprises at least 200 mM NaCl.

add A1

add B1